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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/586,479	06/01/00	SCHMIDT	A 15280-414000

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TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO CA 94111-3834

EXAMINER	
BROWN, S	
ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 07/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/586,479	SCHMIDT ET AL.	
	Examin r	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *68-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 June 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1648. Your application has been reassigned to examiner Stacy Brown.**

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-67, drawn to an isolated infectious human-bovine chimeric parainfluenza virus, a method for stimulating the immune system of an individual and an immunogenic composition to elicit an immune response against PIV, classified in class 424, subclass 184.1.

II. Claims 68-80, drawn to an isolated polynucleotide, classified in class 514, subclass 44.

III. Claims 81-83, drawn to a method and vector for producing an infectious attenuated chimeric PIV particle, classified in class 435, subclass 69.1.

The inventions are distinct, each from the other for the following reasons:

a. Inventions I and II are different products and methods that have different uses and outcomes. Invention I is drawn to a chimeric virus for stimulating an immune response. Invention II is drawn to polynucleotides that encode the chimeric virus of invention I. The virus and the polynucleotides have chemically different structures and perform separate functions such as encoding proteins and eliciting immune responses. The products are not disclosed as capable of use together.

b. Inventions I and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the chimeric virus can be made by another and materially different process, such as chemical synthesis.

c. Inventions II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleotide can be used in a materially different process of using such as inducing an immune response by administering the nucleotide to an individual.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Jeffrey King on May 25, 2001 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-67. Affirmation of this election must be made by applicant in replying to this Office action. Claims 68-83 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

3. The specification is objected to because references to amino acids positions must be accompanied by a corresponding SEQ ID NO. For example, see page 15. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-57 and 63-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 56 recites "The chimeric PIV of claim 1 which is a virus." This claim is unclear because PIV is parainfluenza virus; stating that PIV is a virus is redundant.

b) Claim 57 cites "The chimeric PIV of claim 1 which is a subviral particle." This claim is unclear because PIV is a virus, not a virus particle.

c) Claim 63 and depending claims 64-67 recite "immunogenically sufficient amount", however it is not clear what is meant by this phrase. Without an endpoint (such as eliciting antibodies) it is not known what the immunogenically sufficient amount intended is.

Clarification is required to overcome this rejection.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy et al (WO 98/53078).

a) **Claims 1-6** are drawn to an isolated infectious human-bovine chimeric parainfluenza virus (PIV) comprising a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV background genome or antigenome of a human PIV or bovine PIV combined with one or more heterologous gene(s) or genome segment(s) or a different PIV of a different PIV to form a human-bovine chimeric PIV genome or antigenome, wherein the heterologous gene(s) or genome segments(s) encodes one or more of PIV N, P, C, D, V, M, F, HN and or L protein(s) or fragment(s) thereof, and additionally (claim 3) wherein the heterologous gene(s) or genome segment(s) encodes a complete open reading frame of one or more of PIV N, P, C, D, V, M, F (a glycoprotein), HN and/or L protein(s). The heterologous gene(s) or genome segment(s) includes a heterologous regulatory element. **Claims 7-10** are drawn to the chimeric PIV of claim1, wherein a heterologous gene or genome segment is substituted for a counterpart gene or genome segment in a partial PIV background genome or antigenome. The gene or segment is added adjacent to or

within a noncoding region of the partial or complete PIV background genome or antigenome. The gene or segment can also be added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete PIV background genome or antigenome. Further, the gene or segment can be added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete PIV background genome or antigenome.

Murphy et al disclose infectious PIV wherein the genome or antigenome is modified to yield a chimera of a human PIV and bovine PIV genomic or antigenomic sequence, see page 10, lines 7-11. The recombinant genome or antigenome may be comprised of nucleoprotein (N), phosphoprotein (P) and large polymerase protein (L), fusion protein (F), hemagglutinin-neuraminidase glycoprotein (HN), matrix protein (M), and products of the C, D and V open reading frames of PIV, see pages 18-19, bridging paragraph. Mutations are introduced in various combinations in any of the above mentioned proteins, and also at extragenic sequences such as in the 3' leader or trailer regions of a PIV genome and cis-acting elements (start and end), see page 28, lines 2-10 and page 29, lines 34-37. Additionally, Murphy et al disclose that the recombinant vector (genome) comprises an operably linked transcriptional unit having a regulatory role in PIV gene expression, such as a promoter, a structural or coding sequence, transcription initiation and termination sequences, see page 19, lines 29-36. **Murphy et al teach, in addition to the human-bovine chimeric PIV described previously, mutations are made within the PIV clone including substitution of heterologous genes or gene segments with a counterpart gene or gene segment in a PIV clone**. The order of genes can be changed, the genome

promoter can be replaced with its antigenome counterpart, or selected gene(s) rendered non-functional by ablation, see page 24, lines 3-18. Also disclosed is the introduction of mutations into the genome or antigenome of infectious wild-type PIV, see page 26, lines 24-26.

Murphy et al do not teach an isolated PIV, however they teach isolated PIV particles and the use of the infectious, attenuated PIV for vaccines. One of ordinary skill would have been motivated to isolate the infectious, attenuated PIV in order to properly prepare it for vaccine administration with a reasonable expectation of success. Murphy et al do not teach the specific locations of gene additions or substitutions of the instant invention, however, Murphy et al disclose that mutations within the recombinant PIV clones may be selected based on their ability to alter expression or function of a selected protein, see page 26-27, bridging paragraph. One of ordinary skill would have been motivated to select mutations based on desired outcomes with a reasonable expectation of success that placement of mutations within known boundaries would have predictable results.

b) **Claims 11-23, 35-40, 42-48** are drawn to the chimeric PIV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete BPIV background genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) from a human PIV. The HPIV genes (glycoproteins HN and/or F, or a segment encoding a cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope thereof) are substituted for one or more counterpart genes or genome segments within the BPIV background genome or antigenome. Claim 15 is drawn to a chimeric which is rBPIV3-$F_H HN_H$. Claims 20-23 are drawn to a chimeric PIV wherein the chimeric genome or antigenome comprises a partial or complete

human PIV background genome or antigenome combined with one or more heterologous genes or genome segments from a bovine PIV, specifically the N protein or open reading frame represented by rHPIV3-N_B. **Claims 24-34, 41** are drawn to a chimeric PIV wherein the genome or antigenome is further modified by introduction of one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant non-segmented negative stranded RNA virus, such as PIV3 JS cp45. Also claimed are specific amino acid substitutions that result in phenotypic changes and alter genes. Genes and open reading frames are deleted in whole or in part, or expression is ablated by mutations. **Claims 49-57** are drawn to a chimeric PIV wherein the vector genome or antigenome is a partial or complete HPIV genome or antigenome and the heterologous pathogen is not from PIV. Also claimed is the chimeric PIV which is a virus and subviral particle. **Claims 58-67** are drawn to a method for stimulating the immune system comprising administering a chimeric human-bovine PIV and a physiologically acceptable carrier. Also claimed is an immunogenic composition.

Murphy et al teach that an infectious PIV intended for administration to a human is a human PIV containing genes or gene segments from a bovine or murine PIV type for purposes of attenuation, see page 36, lines 23-27. Individual genes, gene segments, or single or multiple nucleotides of one PIV are substituted by counterpart sequences from a heterologous PIV or other source, such as a cytoplasmic tail, transmembrane domain or ectodomain, epitopic site or region, binding site or region, active site or region containing an active site, see page 37, lines 10-21. **Murphy et al teach rPIV3.*cp*45L, which incorporates three mutations from biologically derived mutant JS cp45**, see page 41, lines 1-9. Mutations occur in the L protein at Tyr_{942}, Leu_{992} and Thr_{1558}, in the N protein at residues Val_{96} or Ser_{389} or JS *cp*45, in the C

protein at Ile_{96}, in the F protein at Ile_{420}, Ala_{450}, in the HN protein at Val_{384}, also in the 3' leader sequences at nucleotides 23, 24, 28, and/or 45 of JS *cp*45, see page 42, lines 1-17. Murphy et al also teach that the mutations adopted from the biologically derived mutant PIV result in attenuated, or further attenuated, chimeric mutant derivatives, see page 39, lines 15-16. Also disclosed is a nucleotide change that results in further attenuation by encoding an amino acid substitution conferring a temperature-sensitivity phenotype, see page 40, lines 16-17. Murphy et al teach deletions, additions, or rearrangement of PIV N, P, L, M, HN, F, C, D, or V gene or gene segment, and also deletions of C, D, or V open reading frames to yield a recombinant PIV having novel phenotypic characteristics, see page 30 lines 26-27 and page 42, lines 24-35. Also, additional genes or gene segments are inserted into the PIV genome or antigenome, such as interleukins and proteins rich in T helper cell epitopes, see page 31, lines 1-6. **Murphy et al teach an infectious chimeric PIV wherein the human PIV is modified to express genes or gene segments from other heterologous sources other than PIV, such as RSV or measles virus**, see page 36, lines 15-24. Also taught are subviral particles (incomplete virus) and viruses, see page 19, lines 26-29. **Murphy et al teach chimeric human-bovine PIV vaccines** administered in a variety of ways (aerosol, droplet, oral, topical) and in a dose from about 103 to about 106 PFU or more of virus per host, see page 43, lines 22-26 and page 44, lines 5-14. Also taught are multiple administrations where different serotypes are administered separately, see page 45, lines 4-9.

Murphy et al do not specifically teach the substitution of bovine HN and N for human HN and N, (or vice versa) however, they disclose human PIV1 and 3 exchanging HN and F proteins, see page 39. One of ordinary skill would have been motivated to

combine human and bovine genes or gene segments because Murphy et al also teach that genes from human bovine PIV can be substituted for each other, see page 36, lines 23-27 and pages 37-38, bridging paragraph. One would have had a reasonable expectation of success given the homology between HPIV3 and BPIV3.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

6. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stacy S. Brown
June 29, 2001

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER